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RADIUM

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VOL. X JANUARY, 1918 No. 4

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A MONTHLY JOURNAL DEVOTED TO THE CHEMISTRY PHYSICS AND THERAPEUTICS OF RADIUM AND RADIO-ACTIVE SUBSTANCES

RADIUM

A MONTHLY JOURNAL DEVOTED TO THE CHEMISTRY, PHYSICS AND THERAPEUTICS OF RADIUM AND RADIO-ACTIVE SUBSTANCES.

Edited and Published by Charles H. Viol, Ph. D., and William H. Cameron, M. D. with the assistance of collaborators working in the fields of Radiochemistry, Radioactivity and Radiumtherapy.

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VOL. X JANUARY, 1918 No. 4

REVIEWS AND ABSTRACTS

Hugh Hampton Young, M. D., (Baltimore), The Use of Radium and the Punch Operation in Desperate Cases of Enlarged Prostate. Annals of Surgery, LXV., pp. 633-641, May, 1917. From the James Buchanan Brady Urological Institute, John Hopkins Hospital. With 14 illustrative figures and diagrams.

"In the treatment of cases of prostatic hypertrophy one is frequently confronted with severe complicating conditions which require most careful study and treatment before an operation to cure the obstruction to urination can be carried out. The kidneys are so frequently injured by long standing back pressure that the phthalein test shows in more than 40 per cent. of the cases an impairment requiring drainage for a more or less protracted period and forced water by mouth to restore them to a sufficiently good condition for operation. The heart is also frequently involved as a result of the renal lesions, but both kidneys and heart usually improve rapidly on appropriate preparatory treatment so that perineal prostatectomy can be carried out without danger."

"The ordinary valvular lesions and moderately severe myocarditis are usually not sufficient to contra-indicate perineal prostatectomy, though care should be taken both in the preparatory care of the patient and in choice of anæsthetic—which should be ether in such cases. A quick operation and thorough packing of the wound to prevent loss of blood is sufficient to carry them through safely. It is often amazing to see how well they convalesce and in not a few instances the heart is benefited by the removal of a focus of infection in the prostate. Occasionally we meet with very severe cardiac conditions which do not clear up or improve sufficiently under careful hospital treatment to warrant the risk of a serious operation. Such cases usually go unoperated and unrelieved, and it is with the idea of furnishing a new means of curing such cases of urinary obstruction that I am presenting the following case:

"The patient arrived at the hospital in desperate condition. An enlarged prostate with 1300 c.c. residual urine had led to great impairment of the kidneys, and severe degeneration of the heart which was in such bad condition that the patient came near death several times during the nine months of treatment which he underwent. It was evident early that a serious operation was out of the question. Anæsthesia also would have been too dangerous, and various cardiac experts who saw him agreed that a major operation would kill him.

"We therefore determined to attempt to cause atrophy of the prostate and shrinking of the intravesical lobes by simple means—radium and fulguration—and the history will show that this was remarkably successful. But as the obstruction to urination still persisted, it was finally decided to carry out a "punch operation" through the urethra to remove the obstructing collar which remained at the prostatic orifice. This was entirely successful—no further catheterization was required and normal urination has been restored—now of eight months' standing.

"Along with this has come a wonderful betterment of his general health, but as the details are important both to surgeons, internists and pathologists, I will give the history of the case in full:

"Case History.—H. M. H. (No. 4413), aged fifty-three, single, admitted June 2, 1915, complaining of frequent and painful urination, and at times incontinence, fluttering of heart, weakness, nausea and vomiting."

"*Family History.*—One sister had cancer."

"*Past History.*—Scarlet fever, diphtheria and mumps as a child. Measles at the age of thirty years. Pneumonia four years ago. No history of tonsillitis, but for the past five years has had shortness of breath, palpitation and fluttering of the heart on going up stairs and on arising in the morning. No pain and no œdema, but considerable nausea often associated with vomiting. Suffers greatly from dyspepsia and often has severe gastric crises. No history of lues or urethritis."

"*Present Illness.*—About five years ago began to have difficulty and frequency of urination. The obstruction has slowly grown worse, and during the past year the frequency of urination has increased greatly and of late there has been occasional incontinence. For four weeks he has suffered considerably with pain in the bladder, strangury, and, during the last two days, with hæmaturia. His general health has been greatly impaired. He has much dyspepsia, stomachic distress, nausea, vomiting, cardiac irregularity, palpitation and loss of weight. At present he voids urine from 2 to 7 times at night and very frequently in the day, often associated with urgency, burning and pain on urination, and hæmaturia. He has never been catheterized."

"*Examination.*—The patient is tall, thin, pale and feeble. The chest is symmetrical; percussion note hyperresonant, and breath sounds high pitched and rather harsh. Vocal fremitus normal and no rales present. Heart much enlarged. P. M. I. is seen 11 cm. from M. S. L. in fifth I. S. R. C. D. extends 11.5 cm. to the left and 3.5 to the right of the M. S. L. The sounds are rather clearly heard at apex, but extremely irregular, skipping a beat about every 9 or 10 beats. Many beats do not appear to reach the wrist. Over the base of the heart the sounds are pretty well heard and the A-2 seems to equal P-2 in intensity. Pulses are easily felt and appear synchronous, though many of the beats heard at the apex do not reach the wrist. The tension and volume ap-

pear rather low and artery wall is perhaps slightly thickened. Blood-pressure, 128-80.

Abdomen: Full, rather distended, with a high-pitched, tympanitic note throughout. Liver dulness extends from fifth rib to 2 f.b. above the costal margin. Spleen is not felt, liver edge not felt. Kidneys, not palpable. No masses nor tenderness.

Genitalia: Negative.

Rectal: The prostate is moderately hypertrophied, rounded, smooth, slightly indurated. Both seminal vesicles are slightly indurated.

Catheter: Residual urine 1300 c. c.

Cystoscopy: Both lateral and median lobes are enlarged. The median lobe is quite prominent and obscures most of the trigone. The bladder is markedly trabeculated, and on the left side the orifices of cellules and diverticula are seen.

Urine: Amber, acid, specific gravity 1010, no sugar, albumin a trace.

Microscopically: Red and white blood corpuscles and bacilli.

Leucocytosis: 13,600. Phthalein test: appearance time, fifteen minutes; first hour, 12 per cent.; second hour, 15 per cent.; total, 27 per cent. Blood urea :0.576 gramme per litre.

Clinical Impression.—The patient is a weak sick man with bad heart and impaired kidneys, due to great back pressure from enlarged prostate. Much gastro-intestinal disturbance. Needs very careful preliminary treatment, continuous catheter drainage, water in large amounts and cardiac therapy. Operation now absolutely contra-indicated.

Treatment.—Rest in bed, continuous catheter drainage, forced water. Digitalis p.r.n.

June 7, 1915: Patient much exhausted, heart weak, greatly troubled with abdominal distention. Phthalein test yesterday showed a marked drop; appearance time forty minutes, first hour, 2 per cent., second hour, 12.5 per cent., total, 14.5 per cent. (drop of 12.5 per cent.).

June 12, 1915: Slightly improved. Now taking digipuratum b. d. until 12 doses are taken. Cardiac condition better.

June 15, 1915: Comment, "Phthalein test not improving, heart bad, anæthesia and prostatectomy would surely invite fatal ending. It is therefore decided to try radium, with the hope that atrophy of the prostate and relief of obstruction to urination will result."

June 16, 1915: *First radium treatment*: 1709 mg. screened by lead covered with 3 inches of gauze and rubber tissue, applied over the perineum. Treatment carried out by Dr. Burnam for eight hours.

June 17, 1915: Patient somewhat exhausted. Pulse a little better. Blood urea improved, now .348 gm. per litre (drop from .576). Phthalein 21 per cent. for two hours.

June 19, 1915: Fulguration applied to middle lobe through cystoscope.

June 26, 1915: Retention still complete. Second fulguration.

June 27, 1915: Phthalein test: appearance time, twenty-six minutes, first hour, 5 per cent., second hour, 10 per cent., total for two hours, 15 per cent. Blood urea, .35.

July 3, 1915: Cystoscopy: The median and posterolateral portions of the prostate are distinctly smaller and are covered with a grayish slough. The left posterolateral portion is more prominent and is fulgurated to-day for five minutes.

July 4, 1915: Retention still complete. Fourth fulguration (median lobe).

July 5, 1915: *Second radium treatment*: 1709 mg. screened as before, applied over lower end of sacrum five hours, over suprapubic region five hours.

July 13, 1915: Retention still complete. Fifth fulguration of prostate.

July 20, 1915: The patient has been wearing a retention catheter up to this time. Retention still complete. General condition, especially heart, greatly improved. Phthalein test shows steady improvement since primary drop after insertion of catheter; is now: appearance time, thirteen minutes, first hour, 14 per cent., second hour, 19 per cent., total, 33 per cent. Blood urea, 0.36.

Rectal examination: The prostate is distinctly smaller and less rounded.

July 22, 1915: *Intra-urethral applications of radium begun*: 103 mg. screened with a platinum capsule 2mm. thick (26-F. in diam.) inserted with a special instrument. (See H. H. Young, The Use of Radium in Cancer of the Prostate and Bladder, J. A. M. A. pp. 1174-77, April 21, 1917, Reprinted in Radium, June 1917. Ed.) so that radium lay within the internal sphincter, and against the anterior surface of the median lobe. Duration of treatment forty-five minutes.

July 26, 1915: Patient up in chair two days and catheterizing himself. Œdema of legs and scrotum for first time.

August 7, 1915: *Resume*: Patient still has complete retention. Is able to void small amounts, but only after considerable straining. He is using a catheter at four to six hour intervals, removing between 400 and 500 c.c. On rectal examination the prostate is small, flat, soft, and one would not judge from the rectal examination that there was present any hypertrophy whatsoever.

Cystoscopic examination shows the bladder mucous membrane slightly congested, the trabeculations are well marked, particularly posteriorly, and today one can see the inter-ureteral muscle which, up to this time, has not been visible. Examination of the vesical orifice shows it slightly irregular, somewhat œdematous. On the right side in the region of the right lateral lobe there is present a well-developed, rounded lobule which evidently projects across the urethra at that point. Posteriorly the edge is small, and there is present only a median bar. On the left side a definite projecting lobe, which was present at previous examination, has apparently disappeared and the margin shows nothing but the irregularities which are due to œdema of the mucous membrane.

August 9, 1915: The patient was examined today, and the lobe on the right side fulgurated vigorously. Patient is going home this evening, and is to return again in about a month. Phthalein test: appearance time, seventeen minutes, first hour, 14 per cent., second hour, 17 per cent., total, two hours, 31 per cent.

October 8, 1915: *Second admission*: Patient has been at home for two months. He has been catheterizing himself 4 to 6 times daily. Retention still complete. Patient very weak and nervous, suffers with frequent nausea and stomachic distress. Cardiac condition has become much worse, now very bad, heart action extremely irregular, pulse 140, irregular in force and rhythm. Apex in sixth interspace 14.5 cm. to left. Area of relative cardiac dulness extends 2.5 cm. to right in fourth interspace, and 15.5 cm. to left in fifth interspace. Sounds at apex cooing in character, second accentuated. No definite murmurs. Chest emphysematous, sonorous rales. Blood-pressure 120-85. Red blood-cells,

4,568,000. Hæmoglobin, 80 per cent. Blood urea, 0.564. Phthalein: appearance time, fifteen minutes, first hour, 12 per cent., second hour, 12 per cent., total, 24 per cent. Urine: cloudy, acid, specific gravity, 1016, albumin a trace, leucocytes, epithelial cells and bacteria.

October 20, 1915: Patient has been very sick, extremely weak, with persistent nausea and vomiting. Heart very irregular and weak. Right radial pulse almost imperceptible today. Left radial very irregular in force and rhythm.

November 30, 1915: During the past month condition has been variable. For the last five days has received digipuratum grs. iii, twice daily. Heart action still quite irregular and rate at apex varies between 80 and 90. Blood-pressure 115/60. Stomach has improved greatly, is gaining in strength. Urinary condition unchanged, still wearing retainer catheter. Phthalein: 24 per cent. in two hours.

December 6, 1915: Pulse has varied between 68 and 80. Digipuratum grs. iii, t.i.d. since November 30. To-day put on grs. iii b.d. General condition improved.

December 14, 1915: Heart much better. General condition fair. Pulse 70, beats forceful, all coming through to wrist now.

December 15, 1915: Retention still complete—inlying catheter. Cystoscope shows a small rounded middle (posterior) lobe, a small prominent anterior lobe, no enlargement of lateral lobes. Prostate per rectum flat, very little broader than normal.

December 16, 1915: Second intra-urethral radium treatment: 103 mg. applied for two and one-half hours in 3 positions in front of middle lobe as shown in chart.

December 27, 1915: Third intra-urethral radium treatment: 103 mg. in thin brass capsule surrounded by rubber catheter, one hour in deeper portion of prostatic urethra and one hour in anterior portion of prostatic urethra, as shown in chart.

January 17, 1916: Fourth intra-urethral radium treatment, with rubber catheter as before, one hour with radium within internal sphincter.

January 24, 1916: Fifth intra-urethral radium treatment, as before, one and three-quarter hours at vesical orifice, and one hour in anterior half of prostatic urethra.

February 21, 1916: *Resume*: During the past eight months the patient has had two massive doses (1709 mg. each) of radium applied from the back and front; five intra-urethral treatments with 103 mg. at a position against the middle lobe or within the internal sphincter seven hours, and in the anterior half of the prostatic urethra two hours; five fulgurations to the middle and lateral lobes at the vesical orifice. (In later cases I have used intrarectal treatments of radium in addition to the intra-urethral.)

As a result the prostate has decreased greatly, but complete retention of urine persists. The kidneys are markedly improved as a result of the catheter drainage, but the cardiac condition, though much improved, is still much too bad to consider any form of prostatectomy under an anæsthetic—the unanimous opinion of consultation of medical and surgical examiners.

The prostate is found to be about normal in size on rectal examination, and the cystoscope shows that the obstruction present is entirely at the vesical orifice, consisting of a small lobule which is directed anteriorly and to the right, and a fairly broad median lobe—the lateral lobes not being enlarged now. With finger in rectum and cystoscope in urethra

the median portion is moderately increased in thickness and there is a firm collar around the shaft of the cystoscope at the vesical neck which is easily palpable."

"*Deductions.*—It seems probable that a *punch operation* would remove this obstruction at the vesical orifice and be sufficient to restore normal urination. Plans are accordingly to be made to carry this out.

These were delayed by an acute "cold" accompanied by renewed cardiac disturbance."

"*Operation* (March 13, 1916) (Young).—Novocaine 4 per cent. in posterior urethra, opium suppository in rectum, punch operation, 8 cuts in all directions around prostatic orifice, commencing with an anterior cut in which a mass of tissue about 1 cm. in diameter was removed. The tissue masses removed by the lateral and posterior cuts were somewhat smaller, with the exception of the right anterior cut in which a mass of tissue about 1 cm. in diameter was removed. The tissue masses removed by the lateral and posterior cuts were somewhat smaller, with the exception of the right anterior cut which apparently removed the lobule previously seen in that location with the cystoscope. There was very little hemorrhage—the clots were easily vacuated with a syringe through a large catheter which was fastened in urethra.

March 4, 1916: Patient had very little shock from operation. There was very little post-operative bleeding, and the heart action remained as good as before. *The catheter was removed in thirty hours, and in a short time urine was voided naturally.*

March 15, 1916: No reaction. Voiding urine freely in amounts from 100 to 300 c.c

March 18, 1916: Continues to improve. Catheter not required. Patient walking about ward.

March 28, 1916: Now two weeks since operation. Convalescence has been remarkably smooth. No cardiac attacks. Has not required catheter since day after operation. *Is now voiding normally, as much as 400 c.c. at a time. General condition excellent. Patient discharged.*

June 15, 1916: Patient returns for observation. He reports continued improvement in every respect. Heart giving very little trouble. Retains urine four hours, voids large amounts each time. Urination normal. Bladder apparently empties itself perfectly. Prostate about normal in size, but slightly indurated. Result excellent."

"*Pathological Report.*—By Dr. Howard Cecil. Path. No. 2350. The tissue removed by the anterior cut is 0.5 cm. in diameter and this small amount of glandular tissue. This section is marked 1. The left anterior cut is 1.5 by ¾ cm. This also contains glandular tissue and the section is marked 2. The left cut is 1.2 cm. in diameter and this section is marked 3. The left posterior cut is 1.2 cm. by 0.5 cm. wide; it contains glandular structure and is marked 4. The posterior cut is 2 by 1 cm. in diameter; it contains what seem to be definite spheroids and is marked 5. The right posterior cut is 1.5 by 1 cm. and is marked 7. The right anterior cut is 2 by 1 cm., the largest of all of the cuts; it contains a fair amount of glandular tissue and is marked 8.

The entire mass shows a definite hypertrophy, but there does not seem to be such a marked amount of connective tissue, though it is fairly hard.

The sections are very similar in appearance and show the following changes: The tissue is extremely rich in epithelial tissue that has undergone a marked degeneration. The section stains a deep blue with

hæmatoxylin. In the acini there are large colloid areas of degeneration. The acini themselves are greatly shrunken, the cells are irregular, generally large, but in places small. The stroma itself has been greatly changed; the cells are vacuolated and the protoplasm has practically all been destroyed. The spheroids here are represented by masses that are very much smaller than normal and definitely encapsulated. There is some epithelial tissue which has undergone a definite colloid change represented by poorly staining blue homogeneous material which, under high power, shows that there is a definite network within the colloid material."

"*Remarks.*—The effects obtained by radium in this case have been duplicated now in several other cases at our clinic—a remarkable shrinking of the hypertrophied gland, with the peculiar tissue changes above described—but also without complete relief of obstruction which generally has remained unchanged, so that radium alone is apparently not a cure for prostatic hypertrophy. The fact that the "punch" operation has been so eminently successful in removing the obstruction remaining after radium treatment at the vesical neck shows a wider use for this procedure which we have heretofore reserved for non-hyperthrophic obstructions at the vesical orifice, bars, valves, contractures and congential obstructions which form so large and troublesome a group of cases."

"By means of specially devised instruments, to be used through the rectum, urethra and bladder—the latter with a cystoscope inside it—it has been possible to get really remarkable results in many cases of prostatic carcinoma—relief of obstruction to urination, disappearance of enlargement, pain and hæmaturia. But the field is too new and the cases too recent to be discussed here. Suffice it to say that in radium we undoubtedly have a therapeutic agent of great value in urology and with improved apparatus, larger amounts of the element (we expect in the future to use 600 mg.) and systematic study of a long series of cases, many brilliant results should be obtainable."

"This report serves to show that with radium the hypertrophied prostate may be made to atrophy so that a minor operation will suffice to restore normal urination. The long duration of treatment, however, suggests that it be confined to cases with severe complicating conditions which preclude perineal prostatectomy, although the latter may be ranked as a benign operation, having a mortality now under 2 per cent."

* * * * *

Isaac Levin, M. D., (New York.) The Prognostic and Therapeutic Significance of Skeletal Metastases in Carcinoma of the Breast. Annals of Surgery, LXV, pp. 326-340, March, 1917.

With regard to Radium and Roentgenotherapy of skeletal metastases, the author says:—

"As stated above, the radical amputation of the breast in the presence of skeletal metastases cannot cure completely the disease. On the other hand, the operation if correctly performed may prolong the life of the patient, since the removal of the primary tumor diminishes the possibility of subsequent formation of metastases in other organs than the bone. But the operation, while aiming at a complete as possible removal of the main mass of the tumor, does not need to be entirely radical.

It is more important not to handle and massage the tumor too energetically during the operation and thereby transport cancer cells into the circulation, than to remove every vestige of it. The writer has shown in a previous publication that small islands of tumor cells can be destroyed by radium and Rontgen rays, even at a great distance from the skin, and it should therefore be easy to eradicate by the aid of the radiations small remnants of the tumor located in the axilla, or over the chest wall. The diathermic coagulation of tissue which the writer discussed in previous publications, and which destroys the carcinoma cells *in situ* without opening the blood and lymph channels, may become the operative methods of choice for such incomplete operations when the correct technic is developed."

"Thus the correct treatment of carcinoma of the breast, complicated with skeletal metastases, consists in the operative removal of the gross tumor mass, combined with radium and Rontgen therapy. The radiations in a postoperative case of carcinoma of the breast should not be given only over the operative field and over the chest wall, which is the procedure generally adopted today, but should include, if not the whole skeleton, at least the spine and the heads of both femurs. Moreover, this combination of surgery and radiotherapy should be the method of choice in all advanced cases of carcinoma of the breast, even when there is as yet no evidence of skeletal metastases."

"The writer has shown that one of the important effects of radium and rontgentherapy consists in the formation of an extensive connective-tissue stroma, surrounding and compressing the tumor cells. In skeletal metastases this stroma, as the pathological study reported above shows, is transformed into bone. It is thus self-evident a *priori* that the radiotherapy must enhance the results of the attempts at cure produced by nature."

"In a case reported by the writer in 1915, though not a metastatic carcinoma, but a primary sarcoma of the bone (right mandible), new bone formed under the influence of radium and Rontgen therapy. Eight weeks after the beginning of the treatment, the tumor had completely disappeared, and instead there was present a large cavity lined by a shell of bone. A rontgenogram is shown taken immediately at the beginning of the treatment, with the radium tubes *in situ*. There is seen a nearly complete loss of bone around the tumor. A rontgenogram taken after treatment, shows that the swelling is surrounded by a great deal of new-bone formation. The Cases IX and X of the present report clearly show that radium and rontgenotherapy may cure clinically skeletal metastases of carcinoma. Case IX is clinically well and shows no recurrence in other regions of the body for two and a half years."

"Case X is now clinically well one year after admission to the hospital, while a year ago it presented the picture of a most hopeless condition, ever met even among cases of inoperable carcinoma. Though it cannot be stated as yet for how long the patient's life will be prolonged, the achievement in this case is certainly sufficient to encourage further attempts at the same method of treatment."

"It would lead too far to go here into details of the technic of radiotherapy, but one point must be considered, the treatment must be continued at stated intervals for a long time, and if it is interrupted too soon, the metastatic tumor may become active again, destroy a large area of bone and then the subsequent radiations will be of no avail."

* * * * *

Henry H. Janeway, M. D. Radium Therapy in Cancer. With the Discussion of Treatment of Cancer of the Bladder and Prostate, by Benjamin S. Barringer, M. D., and an Introduction upon the Physics of Radium, by Gioacchino Failla, E. E., A. M. Paul B. Hoeber (New York) 1917, pp. 242.

We quote from the preface with regard to the objects which the authors have had in mind in preparing this book—

"The somewhat detailed character of the present report has been determined by the urgent need of more accurate descriptions of the methods of applying radium to malignant tumors in different situations. The great majority of available reports indicate the total amount of radium employed, but details regarding concentration of radium to the unit of surface, the exact nature of filtration, the exact periods of repeated applications, and the successive steps of the therapeutic result, are incompletely presented or entirely omitted. Consequently it has been impossible for the reader to duplicate the method or to obtain the necessary information to guide him in his own work. Unfavorable results are experienced in all large radium clinics, but under exactly what circumstances such results may be expected, or how they may be avoided, has seldom been stated. Such information, it is believed, may be obtained from many of the case records of the present report."

"It has become more and more apparent that the successful use of radium in cancer, requires careful consideration of each particular type of the disease in each organ as separate problems, in which different methods must be devised and different results expected. Hence the various forms of cancer are separately considered, and the indications, methods, complications, and results are given briefly for each."

"In our own experience the use of radium emanation has greatly increased the efficiency of radium therapy as compared to the use of the metal itself."

"For a satisfactory understanding of these advantages as well as the principles of application and filtration an acquaintance with the physics of radium is indispensable. It has therefore been deemed advisable to include in this report an introduction explaining in detail the physical considerations relative to the therapeutic application of radium."

In the first chapter Mr. Failla discusses physical considerations relative to the application of radium, treating briefly of such points as Roentgen Rays, Radio-activity, Collection of Radium Emanation, Radio-active Deposit, Properties of the Radiations, Absorption of Radiations, Secondary Radiations, Chemical Actions, Therapeutic Uses, Applicators, Radiation from Typical Applicators and "Dosage".

In the second part Dr. Janeway considers the principles and methods of application of radium to cancer, various forms of applicators used, the technic of radium application and the results of radium treatment in cancer of the lip, tongue, mouth, tonsil, pharynx, larynx, esophagus, stomach, rectum, penis and vulva, uterus, breast, cervical lymph nodes, and skin, parotid tumors, teratoid carcinoma of testis, sarcoma, treatment of gliomata, and nevi.

In the third part of the book Dr. Barringer briefly discusses the radium treatment of bladder and prostatic carcinoma, his report being based on 25 cases of carcinoma of the bladder and 30 cases of carcinoma of the prostate.

This report is one of the most pretentious which has appeared in this

country, and since it represents the results of careful investigations, it is a valuable contribution to the literature of radium therapy. The exactly detailed case reports, describing the technic of application and the dosage, will be of great value to those who are engaged in radium therapy or are taking up work in this field.

* * * * *

Howard A. Kelly, M. D., and Curtis F. Burnam, M. D., (Baltimore.) Treatment of Lymphosarcoma with Radium. Southern Surgical and Gynecological Association, December 15, 1915.

Dr. Kelly and Dr. Burnam, pointed out the differences between lymphosarcoma and Hodgkin's disease and the various leucemias. They drew attention briefly to the history of lymphosarcoma, beginning as a local infection and growing more or less rapidly, metastasizing, and finally invading the lymphatic system, more or less, of the whole body, and invariably causing death in a period of from several months to a couple of years. Surgery had always stood impotent in the presence of lymphosarcoma, even in such an accessible region as the neck, and when situated in the breast or abdomen it was, of course, even beyond the dream of surgical relief. It was Nicholas Senn who, in 1903, opened up the great question of the ray therapy of these affections.

A series of twenty cases was presented, all but two identified by a microscopic examination of the tissues. Most of the patients were in an extremely advanced stage of the disease, and twelve had been operated upon, and these, with one exception, were sent as a last desperate hope with rapidly recurring masses in the neck. Out of that group of twenty, thirteen or sixty-five per cent. were apparently cured. Six patients had died of the disease, five of that group had been operated upon, and all had advanced cases but one. On the basis of this experience they believed that lymphosarcoma ought not in the future to be operated upon, but should be subjected to radium therapy at the earliest possible moment. The results were found to improve if the cases were obtained early, and they confidently expected to increase their percentage of recoveries from sixty-five to ninety per cent. or over.

The amounts of radium used varied from 441 mgs. to 2,000, distributed over different areas for several hours, and repeated at intervals of weeks or months. While in the early cases the diseased area alone was treated, in the later cases the entire lymphatic system of the neck, axillæ, and torso had been included. There were several instances of primary extensive lymphosarcoma of the mediastinum. Those responded just as readily as those more superficially placed.

In view of those results and the rescue by radim of this most distressing malady from the realm of the incurable, all future cases should have the benefit of a thoroughgoing radium treatment at the earliest possible moment.

Dr. J. Louis Ransohoff, Cincinnati, Ohio, in discussing the above paper, said that he and Dr. Joseph Ransohoff had been using radium for three years. While using a limited amount of radium as compared with Dr. Kelly, nevertheless, they are able to substantiate from their experiences the beautiful results which Dr. Kelly had shown. It is necessary, however, when having a limited supply of radium on hand to adopt a rather different technic. Dr. Kelly referred to enormous lymphosarcomata having disappeared after being treated for two or six hours at

different sittings. Having a limited amount of radium at one's disposal, possibly one can do the same thing exactly by dividing the tumor off into certain areas, blocking the tumor on the history chart, and making a note each time or each day where you apply the radium so as not to go over the same ground twice. Instead of using the radium so many seconds, it can be left from 24 to 48 hours. It remains to be seen, of course, whether smaller doses applied in this way will take the place of the enormous massive doses which Dr. Kelly has been able to use. It is fortunate if these results can be obtained with the smaller doses as it permits a greater number of investigators to thoroughly find out the true status of radium and its value in surgery.

Dr. Ransohoff had three cases of lymphosarcoma which were treated with radium a little over two years ago. The patients are still well. Two other cases that are apparently cured, are too recent to speak of as other than apparent cures, although, as Dr. Kelly has said, there is no real cure until five or six, or even seven years have elapsed, and perhaps not even then.

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Irving Sobotky, M. D., (Boston). Radium Treatment of Tinnitus and Middle Ear Deafness. N. Y. Med. Jour., CV, pp. 1138-39, June 16, 1917.

"Realizing the futility of attempting to cure tinnitus of long standing or middle ear deafness by catheterizing the Eustachian tubes, the writer decided to experiment with radium. The use of radium in ear conditions, while not new, is recent. Bruhl and Albrecht, in Berlin, report a series of cases in 1914, as did Hugel and Haelin. Bruhl and Albrecht used massive doses of radium and considered a patient benefited only if the perception of whispered words was increased. They placed as far as possible in the ear canal a measured quantity of radium in the form of a radium bromide applicator. The radium strengths used were two milligrams, 7.75, and in a few cases twenty-three milligrams. The ear canal was protected by a thin layer of tinsel paper. The exposure could thus be made for ten to thirty minutes with a minimum of dermatitis. As a rule the radiation was repeated every eight days and was interrupted after three exposures. Their conclusions were: 1. Radium has no beneficial influence upon hearing. 2. Radium benefits and even cures tinnitus. 3. Radium disturbs the ear nerve mechanism without harming the other structures. 4. Radium relieves dizziness."

"Hugel, however, using five milligrams of radium, reported twelve cases of deafness benefited out of nineteen radiated. Haelin's results seem to agree with neither of the other observers. He reports eleven cases of deafness treated, with one improved and eleven cases of tinnitus with five improved. W. S. Bryant, of New York, has reported excellent results in a number of cases treated with large doses of mesothorium."

"Not having a massive quantity of radium at his disposal, the writer used a 0.0001 gram radium sulphate applicator. This applicator consists of a small bead about the size of a buck shot, the radium being enclosed in substance within a glass capsule. A flexible wire is fused into the head. This applicator is inserted unscreened into the ear canal, and gently pushed inwards, under eye guidance, until the capsule is in contact with the tympanum. The flexible wire allows the applicator to be in-

serted into the most tortuous canals. The applicator is held in place by a bit of cotton put into the meatus. The first treatment is of thirty minutes' duration, and the following sittings are gradually increased up to one hour. The patients experienced no discomfort, except in three cases, when a slight itching of the ear canal occurred. This is in contrast to the powerful applicators which often produce skin burns."

"By using radium unscreened and in direct application to the tissues the rays are not filtered either by interposed metal or through distance. The entire rayage is thus utilized minus the alpha particles; none of those penetrate the glass; but the gamma rays and a considerable amount of the beta rays do penetrate. It is probable that by using the apparatus unscreened, its power was somewhat increased, because of the greater proportion of beta rays. Latterly the views of physicists are being modified in the direction of greater employment of the beta rays. This end one secures by close application—no distance filtration—and by leaving out interposed metal. It is even contended that the beta rays are of more importance than the gamma. According to this view the gamma rays are affective by virtue of their creating secondary beta rays on contact with the tissue."

"The amount of radium used by the writer was small and could not be considered in neoplastic cases where it would be necessary to affect cell growth. In ear cases the amount of pathology is small, its character relatively simple, the aural apparatus delicate, and in a small compass. What we have to deal with are the end results in slowly progressive, low grade, inflammatory process. In such cases the primary influence of radium we are seeking is its stimulating effect. Small doses of radium stimulate, large doses affect the cells of living organisms. A small amount of radium may procure the resorption of inflammatory products, first by stimulating phagocytosis and second by its influence on sensory nerves in the regulating of the blood supply."

"The results, while not at all brilliant, are, as shown below, encouraging and interesting from the experimental point of view. The following cases were radiated at the Massachusetts Charitable Eye and Ear Infirmary. The hearing was tested before radiation was started and at the discontinuance of treatment. These tests were done by an intern who had no knowledge that the patients had received special treatment. The patients were gathered from both infirmary and private practice."

"Case I.—Girl, age twenty years, employed in a factory. Diminished hearing for past two years. Hearing test, before radiation: Right, whisper, 8 feet; voice, 25 feet; Rinne, 14-18 seconds; Low, 64 fork. Weber, > left; whisper, 6 feet; voice, 15 feet; Rinne, 4-12 seconds; Low, 128 fork."

"After twenty-two radiations, left ear only: Left, whisper, 8 feet; voice, 19 feet; Rinne, 6-12 seconds; Low, 128 fork. Right, Weber, > . Rinne, 11-18 seconds."

"Case II.—Housewife, aged thirty years. Diminished hearing past five years. Severe tinnitus. Hearing test before radiation: Right, whisper, 3 feet; voice, 25 feet; Rinne, 3-17 seconds; Low, 96 fork. Weber, > left, whisper, 0; voice, 0; Rinne, 0-13 seconds."

"After twenty-five radiations there was no change in her hearing. The tinnitus was relieved."

"Case III.—Boy, aged eighteen years. Hearing test before radi-

ation: Right, Weber, < whisper, 0; voice, 0; Rinne test 0.5 seconds. Left, whisper, 0; voice, 0; Rinne, 0.4 seconds."

"After twenty-one radiations he could hear a shout, but could not distinguish the word. A 512 fork was heard by air conduction for one second."

"Case IV.—Housewife, aged thirty-two years. Hearing test before radiation: Right, whisper, 4 feet; voice, 25 feet; Rinne, 24-10 seconds; Low, 80 fork, and Weber, > left, whisper, 3 feet; voice, 25 feet; Rinne, 15-11 seconds; Low, 128 fork.

"After forty-two radiations, left ear only; Right, whisper, 4; voice, 25; Low, 80; Weber, > Rinne, 25-12 seconds. Left, whisper, 3; voice, 25; Low, 128; Rinne, 21-15 seconds."

"Total cases of chronic secretory otitis media treated for defective hearing, twenty-five. Cases of tinnitus treated, twenty-five.

"*Results*—Defective hearing: cured, none; improved, five; not improved, fourteen; worse, six. Tinnitus: cured, one; improved, ten; not improved, twelve; worse, two."

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W. H. B. Aikens, M. D., (Toronto.) The Radium Treatment of Malignant Disease of the Lip and Skin. Canadian Practitioner and Review. XLII, pp. 142-148, April 1917.

"The treatment of malignant disease of the lip and skin may be considered from several points of view. Cancer of the skin, more particularly when it involves the lower lip, frequently attains a high degree of malignancy, and appears to be a regional rather than a local process, the neighboring glands being usually affected. As it is generally preceded by a pre-cancerous lesion of some kind, such as a scaly spot, excoriation, wart or mole, it follows that the persistence of such lesions for an unduly prolonged period should excite suspicion, and lead to the adoption of prophylactic treatment, in which radium applications are of great value."

"Until comparatively recently the best routine treatment of cutaneous epithelioma was by an early operation, and in this way it is possible to remove the growth in many cases. In epithelioma of the mouth and lower lip, however, the diagnosis is seldom made before the adjacent lymphatics are involved, and anything like complete excision is therefore impossible, in a large number of cases, owing to the extent of the growth and the nature of the tissues invaded. The frequency of early metastasis in these cases will be apparent from Murphy's statement that in a series of cases of epithelioma of the lower lip 52 per cent. without demonstrable metastasis at the time of operation and 76 per cent of those who showed enlargement of the glands at the time of operation, subsequently died of cancer."

"Since the introduction of radium into the field of therapeutics, treatment by radium rays has come to be the method of choice in cutaneous epithelioma. Amongst its advantages are the ease of application and lack of discomfort to the patient with which it can be applied, the complete destruction and eradication of the cancer cells, the stimulus to healing induced by the rays, and the excellent cosmetic results,

which are far superior to those after operation or caustic applications, which leave a large and retracted scar."

"Epithelioma of the skin seems to form an exception to the general rule that operable cancer should be operated upon, as in many cases the better cosmetic results and the comparative infrequency of recurrence after its use, render radium treatment preferable to surgery, and many are now of opinion that operation should be undertaken only in exceptional cases."

"Before applying radium, however, it is now my invariable practice to curette away as much as possible of the cancerous tissue."

"In a recent paper Dr. Frank E. Simpson, (J. A. M. A. Nov. 18, 1916. p. 1508) discusses the difference in the action of radium and x-rays. Both have a selective and inflammatory reaction. In regard to the x-rays the former is much the most important, there being considerable risk in the systematic production of a destructive inflammatory reaction by them. Radium on the other hand, when used with proper precautions, is a valuable destructive agent, and it has been proved conclusively that it is capable of destroying the epitheliomatous tissue. As our object in treatment is to completely eradicate every cancerous cell, and nothing short of this is likely to be effective in preventing recurrence, this destructive action of radium is of the greatest significance in this connection, more especially in view of the frequency of recurrence after surgical operations, even when they include wide removal of the adjacent tissues. From a cosmetic point of view also it is preferable to surgery in many cases, in which operation would entail considerable disfigurement and mutilation, such as epithelioma in various parts of the face."

"Observers everywhere are now agreed that radium is the ideal method of treatment in cutaneous cancer, and during the twelve years which have elapsed since its introduction evidence has continued to accumulate as to its remarkable efficacy in these conditions. The results in some of the cases reported have been simply marvellous, and cases in every stage of the disease, even the most advanced, have yielded to treatment, sometimes after proving refractory to all other methods."

"Dr. W. B. Chase, (Med. Record, XC. p. 410, 1916) reports a case in which an extensive epithelioma of the face disappeared after three applications of radium, as did also another affecting the face and another the hand. In large cutaneous epithelioma he plunges needles containing radium into the growth. He has found this form of treatment beneficial in several cases, and is of opinion that it is likely to prove preferable to other methods. A case of mammary epithelioma in a woman of 80, entirely disappeared after it two years ago, and has since remained perfectly healthy."

"Dr. Riddell reports a case of epithelioma of the right temple in a man who had suffered from lupus for twenty-five years, and had x-ray treatment for seven years. A recurring fungating growth was treated by two applications of radium with good results, and up to the time of writing there had been no recurrence."

"In a case reported by Dr. Russell Boggs, (Radium, Nov. 1916) the growth had its origin over the bridge of the nose, involved the canthus, and was destroying the lower lid and conjunctiva. He states that healing is so perfect that it is difficult to believe that such a condition has ever existed."

"An experience of several hundred cases has convinced me that no other agent can compare with radium for the treatment of such lesions. Small rodent ulcers respond almost magically, whilst other more extensive cases, which are of several years' duration, and have resisted all sorts of therapeutic measures, including the x-rays, excision, and various methods of physical therapy, have also been favorably influenced by radium."

"The case reported was not only an intractable epithelioma of long standing, but in addition presented certain other characteristics, which render it of special interest at the present time."

"On May 22nd, 1915, Dr. A. T. Emmerson of Goderich referred to me for radium treatment a patient with the following history:

"He was a man of 61 years of age, at present a mill-hand, but had formerly seen service in the British Army. Eight years previously an ulcer had appeared on his right temple, which had gradually increased in size, and at the time he came to me there was an ulcerated area, roughly circular in shape, extending from the anterior margin of the auricle to half an inch beyond the outer margin of the orbit (three inches,, and from the hair margin above down for two or three quarters of an inch to a point opposite the lower margin of the external auditory meatus. The margins of the ulcer were elevated, and its base irregularly covered with granulations, from which sero-purulent discharge exuded. It proved to be a typical cutaneous cancer."

"A radium plaque 4 centimetres square containing one centigram of radium element was applied over the ulcer, remaining *in situ* for twelve hours. The posterior portion of the ulcer, where the thickening of the edges was most marked, received an exposure of twenty-four hours."

"The patient was sent home after receiving instructions to dress the ulcer with boracic acid compresses. Six weeks later he came to see me again.

"The edges of the ulcer were soft and flattened, except anteriorly, where a slight elevation still persisted. The ulcer had healed with the exception of an area in the centre, one square inch in diameter. The part over which complete epithelialisation had not yet taken place presented the appearance of a clean, healthy ulcer."

"The treatment given on this occasion was the application for fourteen hours of the same radium plaque covered by two millimetres of aluminum. In the anterior portion, where slight thickening persisted on the margins of the older ulcer, a smaller plaque, of similar relative strength, was applied for fourteen hours."

"The patient was asked to report again at the end of another six weeks, but failed to do so, and no further information was received until November, 1916. Dr. Emmerson then wrote to me with regard to a similar case, and in his letter referred to the results obtained with the first patient. I cannot do better than quote from it:

"Mr. F. told me that you had taken a photograph of his face each time he went down. If that is so, then they would be complete if you had one of his face as it is at present time. He is with one of the battalions that is going, or is now on its way overseas. I had him go to a photographer, and he has taken a picture which I send you under separate cover. He did not retouch the negative, thinking it would be better not for the purpose for which you might require it. The picture does not do justice to the healed part. You can understand that the

surface is more or less uneven, also there are one or two large veins running across it. These have given shadows, which account for the unevenness of the picture. The result is excellent, and the skin over it is becoming firm."

"This report was certainly most gratifying. The fact that the ulcer had completely healed was in itself a cause for great satisfaction, but the additional information that the patient had passed a Medical Board as "fit" for service in the Canadian Expeditionary Force considerably increased my satisfaction, and adds a peculiar interest to the case, which has led me to publish it:"

"It now seems to be the general opinion that in epithelioma of the skin we have one of the most promising fields for radium therapy, which often succeeds when other measures have failed to give relief."

"Cases have been recorded in which the use of radium has resulted in improvement, even when metastasis has occurrd before the patient comes under observation. Dr. Casper Gilchrist (Maryland Med. Jour., 1915, 157) reports three cases of the kind. In the first a man of 65 suffered from epithelioma of the wrist, with extensive metastasis to the upper lip and adjacent region. Treatment resulted in healing of the lip and clearing away of the primary cancerous deposit in the wrist, with great improvement in the general condition. In the second case there was epithelioma of the bridge of the nose, with metastasis to the left side of the neck. There was marked improvement, but the patient subsequently died of pulmonary embolism. In the third case there was an epithelioma of the lower lip, with metastasis to the cervical glands and subsequently to the sternum. After treatment by radium the patient was discharged as clinically cured."

"All writers on the subject emphasize the importance of giving prophylactic doses of radium at intervals after apparent cure, and of keeping the cases under observation for a prolonged period, with the object of detecting recurrence at an early stage."

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H. Hausmann, (Wiener klinische Wochenschrift, Vienna., Oct. 11, 1916, XXIX, pp. 1289-1320.) Hemolysis by Radium Rays. Abstract from Jour. A. M. A., LXVIII, p. 72, January 6, 1917.

"Hausmann relates experiences which show that the radium rays are able to hemolyze rabbit red corpuscles suspended in agar plates. This seems to be the work of the beta rays."

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